IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of
Albert Charles GYORKOS et al.
Serial No. : 10/577,334 Group Art Unit : 4121
Filed : April 28, 2006 Examiner : Alicia L. Fierro
For : NITROGEN-CONTAINING FUSED HETEROCYCLIC COMPOUNDS

DECLARATION UNDER 37 CFR Sec. 1.132

Honorable Commissioner of Patents and Trademarks
P.O. Box 1450, Alexandria, VA 22313-1450

Sir,

I, Kazuyoshi ASO, a citizen of Japan residing at 10-5-307, Kamihamuro 1-chome, Takatsuki-shi, Osaka, Japan, declare and say that:

1. I was born on September 11, 1963 in Fukuoka, Japan;
2. I graduated from Kyushu University, with degree of Master of Pharmaceutical Science in March 1989;
3. I have been employed by Takeda Pharmaceutical Company Limited, Osaka, Japan, since April, 1989, and have been engaged in research and development in the Pharmaceutical Research Division of said company;
4. I was a visiting scientist in SmithKline Beecham Pharmaceuticals (Philadelphia, PA) from July, 1996 to October, 1996;
5. I was a visiting scientist in Array Biopharma Inc. (Boulder, CO) from June, 2003 to April, 2004;
6. I have been appointed a Research Head of Medicinal Chemistry Research Laboratories in said Pharmaceutical Research Division since 2004;
7. I am a member of the Pharmaceutical Society of Japan, and published with other research workers, a number of reports on scientific studies, among others, including

1) Competitive Intramolecular [4+2] Cycloaddition and Tandem [2+2]Cycloaddition / [3,3]-Sigmatropic Rearrangement Sequence of Allenyl 3-Vinyl-2-cyclohexenyl Ethers: Evidence for Switching of the Reaction Pathway by the Substituent Effects; *J. Am. Chem. Soc.* 111, 5312-5320 (1989)

2) Synthesis and Antitumor Activity of Pyrrolo [2,3-d] pyrimidine antifolates with a Bridge Chain Containing a Nitrogen Atom; *Chem. Pharm. Bull.* 43,

256-261(1995)

3) Novel Pyrrolo [2,3-d] pyrimidine Antifolate TNP-351: Rapid Uptake and Polyglutamate Formation, and High Affinity for Reduced-folate Transport System in Murine Tumor Cells; *J.Takeda. Res. Lab.* 54, 97-107 (1995)

4) Recombinant *Plasmodium falciparum* dihydrofolate reduced-based in vitroscreen for antifolate antimalarials; *Mol. Biochem. Parasitol.* 81, 225-237 (1996)

5) Enzyme-inhibition system for identifying potential antimalarials that target highly drug-resistant mutants of *Plasmodium falciparum* dihydrofolate reductase ; *Parasitology International* 47, 65-78 (1998)

6) Pyrrolo[2,3-d]pyrimidine thymidylate Synthase Inhibitors: Design and Synthesis of One-Carbon Bridge Derivatives; *Chem. Pharm. Bull.* 49, 1280-1287 (2001);

8. I am one of the co-inventors of the above-identified application Serial No. 10/577,334 and familiar with the subject matter thereof.

9. The Corticotropin-Releasing Factor (CRF) binding inhibitory rates of the example compounds in the present application were measured according to the description of "Experiment 1" in the specification under my supervision and control. The binding inhibitory rates of representative compounds are shown in Tables 1 to 6 attached hereto.

10. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

This 4th day of September, 2009

Kazuyoshi Aso

Kazuyoshi ASO

Table 1

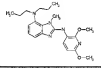
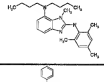
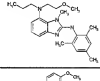
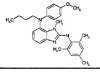
Example No.	Structure	Binding inhibitory rate (%) 1000 nM
30		93.6
35		64.2
44		91.1
47		77.9
54		90.6
55		81.6
56		93.3
58		96.3
59		96.0
69		95.5

Table 2

Example No.	Structure	Binding inhibitory rate (%) 1000 nM
70		90.9
71		94.5
73		88.0
74		95.4
75		82.3
80		90.6
81		100.5
86		95.5
88		96.9
89		99.1

Table 3

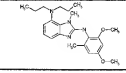
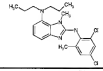
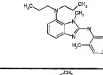
Example No.	Structure	Binding inhibitory rate (%) 1000 nM
90		91.4
93		99.6
94		100.7
97		98.9
99		95.0
101		77.8
102		101.2
104		99.0
109		93.0
113		100.6

Table 4

Example No.	Structure	Binding inhibitory rate (%) 1000 nM
123		95.4
125		99.5
138		92.9
140		86.9
146		98.8
149		94.8
150		90.1
152		89.1
155		104.9
156		97.5

Table 5

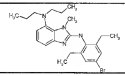
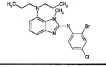
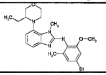
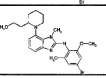
Example No.	Structure	Binding inhibitory rate (%) 1000 nM
157		102.9
158		93.4
159		93.7
160		97.5
163		99.9
164		98.6
165		100.3
166		92.3
167		94.4
169		99.7

Table 6

Example No.	Structure	Binding inhibitory rate (%) 1000 nM
170		98.6
171		102.2
176		93.0
186		79.4
187		86.1
188		84.7
207		93.3